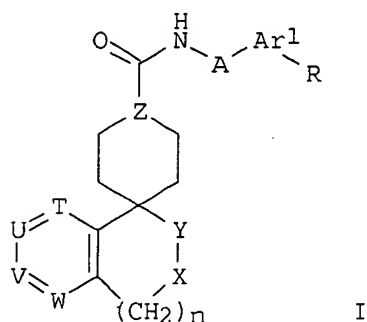


C.A.S- 10-11-03

PATENT INFORMATION:

GT



AB The invention relates to compds. such as spiro[cyclohexane-1,1'-(3'H)-isobenzofuran], spiro[4-, 5-, 6-, or 7-azaisobenzofuran-1(3H),1'-cyclohexane], spiro[indoline-3,1'-cyclohexane], spiro[indoline-3,4'-piperidine], spiro[isobenzofuran-1(3H),4'-piperidine], and spiro[isoquinoline-1(2H),4'-piperidine] represented by the general formula (I) or salts or esters thereof [A = linear C1-6 hydrocarbon group which may be substituted or interrupted by oxygen or nitrogen; Ar1 = (un)substituted aryl or heteroaryl; n = 0,1; R = H, lower alkylene; T, U, V, W = (un)substituted CH or N and at least 2 of T, U, V, and W is (un)substituted CH; X = -N(SO2R1)-, -N(COR2)-, or CO; Y = -C(R3)(R4)-, O, or -N(R5)-; and Z = CH or nitrogen; wherein R1, R2, R5 = H, lower alkyl,

aralkyl, aryl; R3, R4 = H, HO, lower alkyl, aralkyl, aryl]. These compds. exhibit neuropeptide Y (NPY) receptor antagonism and are therefore useful as treating agents for various diseases in which NPY participates such as circulatory diseases, central nervous system diseases, and metabolic diseases, in particular over eating (hyperphagia), obesity, and diabetes. Thus, 64 mg 4-phenylcyclohexylamine hydrochloride and 115 mg 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride were added to a soln. of 74 mg trans-3'-oxospiro[cyclohexane-1,1'(3'H)-isobenzofuran]-4-carboxylic acid in 2 mL pyridine and stirred at room temp. for 24 h to give trans-3'-oxo-N-(trans-4-phenylcyclohexyl)spiro[cyclohexane-1,1'(3'H)-isobenzofuran]-4-carboxamide (II). II and trans-N-[(S)-1-benzyl-2-(benzylamino)ethyl]-1-(methanesulfonyl)spiro[indoline-3,1'-cyclohexane]-4'-carboxamide showed IC50 of 2.5 and 0.69 nM for inhibiting the binding of [125I]peptide YY to human NPY Y5 receptor.

IT 497238-40-1P 497238-44-5P

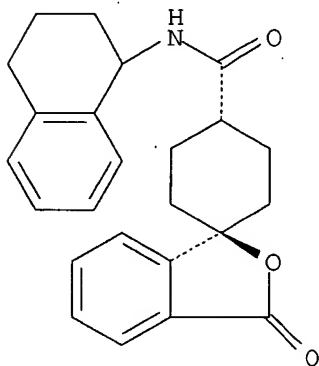
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of spiro[isoquinoline-piperidine], spiro[indoline-piperidine], and spiro[azaisobenzofuran-cyclohexane], and spirocyclohexane compds. as antagonists of neuropeptide Y receptor for treating overeating, obesity, and diabetes)

RN 497238-40-1 CAPLUS

CN Spiro[cyclohexane-1,1'(3'H)-isobenzofuran]-4-carboxamide, 3'-oxo-N-(1,2,3,4-tetrahydro-1-naphthalenyl)-, trans- (9CI) (CA INDEX NAME)

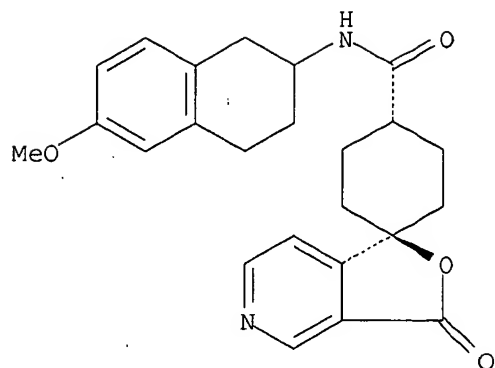
Relative stereochemistry.



RN 497238-44-5 CAPLUS

CN Spiro[cyclohexane-1,1'(3'H)-furo[3,4-c]pyridine]-4-carboxamide, 3'-oxo-N-(1,2,3,4-tetrahydro-6-methoxy-2-naphthalenyl)-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2003:97426 CAPLUS

DOCUMENT NUMBER: 138:137598

TITLE: Preparation of [11C]trans-N-[5-(2-fluorophenyl)-2-pyrimidinyl]-3-oxospiro(5-azaisobenzofuran-1(3H),1'-cyclohexane)-4'-carboxamide (I) as radiolabeled neuropeptide Y Y5 receptor antagonist

INVENTOR(S): Burns, H. Donald; Gibson, Raymond E.; Hamill, Terence G.; Fukami, Takehiro

PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Banyu Pharmaceutical Co., Ltd.

SOURCE: PCT Int. Appl., 29 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003010175	A2	20030206	WO 2002-US23044	20020719

W: CA, JP, US

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR

PRIORITY APPLN. INFO.: US 2001-307499P P 20010724

AB The present invention is directed to radiolabeled neuropeptide Y Y5 receptor antagonists, in particular [11C]trans-N-[5-(2-fluorophenyl)-2-pyrimidinyl]-3-oxospiro(5-azaisobenzofuran-1(3H),1'-cyclohexane)-4'-carboxamide (I), which are useful for the labeling and diagnostic imaging of neuropeptide Y Y5 receptors in mammals (no data). Thus, a 1 mL vial was charged with 0.5 mg trans-4-(3-bromopyridin-4-yl)-4-hydroxy-N-[5-(2-fluorophenyl)-2-pyrimidinyl]cyclohexanecarboxamide and 1.2-1.4 mg Pd(PPh<sub>3</sub>)<sub>4</sub> in 0.3 mL THF, capped, flushed with nitrogen, and shaken until homogeneous for 25 min at room temp. The mixt. was transferred with pressure (35 Mpa) to a microautoclave precharged with [11C]carbon monoxide and heated at 125.degree. and 5,000 psi for 5 min to give I.

IT 494802-27-6P

RL: DGN (Diagnostic use); PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of [11C]trans-N-[5-(2-fluorophenyl)-2-pyrimidinyl]-3-oxospiro(5-azaisobenzofuran-1(3H),1'-cyclohexane)-4'-carboxamide as radiolabeled neuropeptide Y Y5 receptor antagonist for diagnostic imaging)

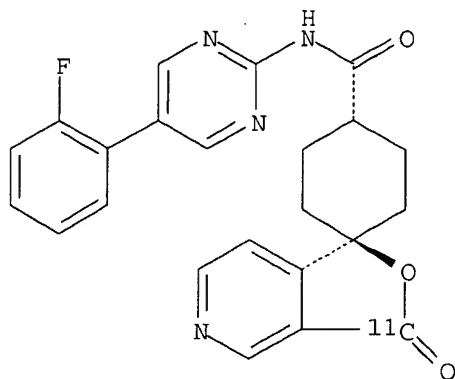
RN 494802-27-6 CAPLUS

CN Spiro[cyclohexane-1,1' (3'H)-furo[3,4-c]pyridine]-3'-11C-4-carboxamide,

10/092,549

N-[5-(2-fluorophenyl)-2-pyrimidinyl]-3'-oxo-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L4 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN  
ACCESSION NUMBER: 2002:947029 CAPLUS  
DOCUMENT NUMBER: 138:24705  
TITLE: Preparation of spiroisindolinepiperidinecarboxamides, spirocyclohexaneisobenzofurancarboxamides, spiroazaisobenzofurancyclohexanecarboxamides, and related compounds as neuropeptide Y antagonists.  
INVENTOR(S): Fukami, Takehiro; Kanatani, Akio; Ishihara, Akane; Ishii, Yasuyuki; Takahashi, Toshiyuki; Haga, Yuji; Sakamoto, Toshihiro; Itoh, Takahiro  
PATENT ASSIGNEE(S): Japan  
SOURCE: U.S. Pat. Appl. Publ., 53 pp., Cont.-in-part of U.S. Pat. Appl. 2002 52,371.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002188124	A1	20021212	US 2002-92549	20020308
JP 2003104884	A2	20030409	JP 2002-271261	20000817
US 6326375	B1	20011204	US 2000-640784	20000818
US 6335345	B1	20020101	US 2001-928431	20010814
US 2002052371	A1	20020502	US 2001-983598	20011025
US 6388077	B2	20020514		
US 6462053	B1	20021008	US 2002-101221	20020320
US 2002165391	A1	20021107		
US 2003055251	A1	20030320	US 2002-226225	20020823
WO 2003076443	A1	20030918	WO 2003-JP2611	20030305

W: AE, AG, AL, AM, AU, AZ, BA, BB, BR, BY, BZ, CA, CN, CO, CR, CU, DM, DZ, EC, GD, GH, HR, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, NO, NZ, OM, PH, PL, RO, RU, SC, SG, TJ, TM, TN, TT, UA, US, UZ, VC, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

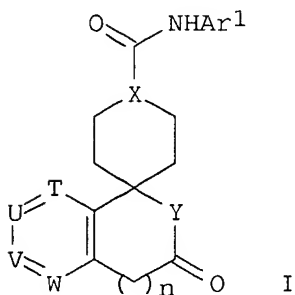
PRIORITY APPLN. INFO.:

JP 1999-233573 A 19990820

10/092,549

JP 2000-137692	A	20000510
US 2000-640784	A3	20000818
US 2001-983598	A2	20011025
JP 2000-247145	A3	20000817
US 2002-92549	A	20020308
US 2002-101221	A3	20020320

OTHER SOURCE(S): MARPAT 138:24705  
GI



AB Title compds. [I; Ar1 = (substituted) aryl, heteroaryl, QAr2; Ar2 = (substituted) aryl, heteroaryl; Q = bond, CO; T, U, V, W = N, (substituted) CH; X = CH, CH(OH); Y = (substituted) imino, O], were prepd. Thus, N-tert-butoxycarbonyl-4-piperidone was refluxed 3 h with PhCH2NH2 in PhMe to give a residue which was stirred with o-iodobenzoyl chloride and Et3N in PhMe at 80.degree. for 2 h to give N-benzyl-N-(1-tert-butoxycarbonyl-1,2,3,6-tetrahydropyridin-4-yl)-2-iodobenzamide. The latter was heated with Pd(OAc)2, Ph3P, K2CO3, and Et4NCl in MeCN at 80.degree. for 6 h to give 2-benzyl-1'-tert-butoxycarbonyl-1',6'-dihydrospiro[1H-isoindole-1,4'(5'H)-pyridine]-3(2H)-one. This was converted to N-(4-benzoylphenyl)-3-oxospiro[isoindoline-1,4'-piperidine]-1'-carboxamide (II), which inhibited [125I]neuropeptide Y binding to NPY Y5 receptors with IC50 = 1.2 nM. II drug formulations are given.

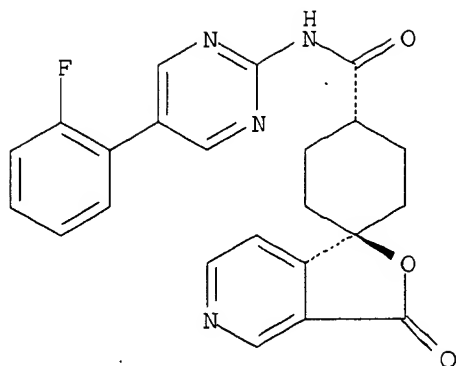
IT 328232-65-1P

RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of spiroisoindolinepiperidinecarboxamides, spirocyclohexaneisobenzofurancarboxamides, spiroazaisobenzofurancyclohexanecarboxamides, and related compds. as neuropeptide Y antagonists)

RN 328232-65-1 CAPLUS

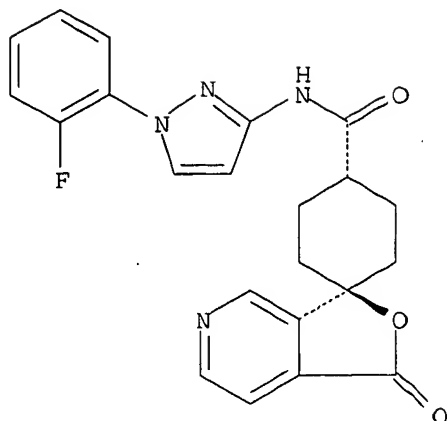
CN Spiro[cyclohexane-1,1'(3'H)-furo[3,4-c]pyridine]-4-carboxamide, N-[5-(2-fluorophenyl)-2-pyrimidinyl]-3'-oxo-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 328232-41-3P 328232-42-4P 328232-43-5P  
328232-44-6P 328232-45-7P 328232-46-8P  
328232-47-9P 328232-48-0P 328232-49-1P  
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10/092,549



IT 478014-38-9P

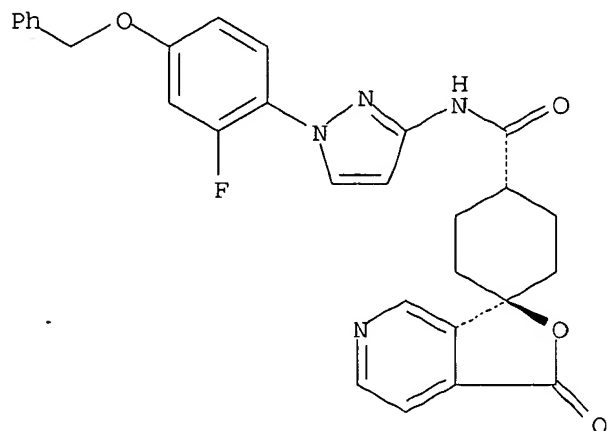
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of spiroisindolinepiperidinecarboxamides, spirocyclohexaneisobenzofurancarboxamides, spiroazaisobenzofurancyclohexanecarboxamides, and related compds. as neuropeptide Y antagonists)

RN 478014-38-9 CAPLUS

CN Spiro[cyclohexane-1,3' (1'H)-furo[3,4-c]pyridine]-4-carboxamide, N-[1-[2-fluoro-4-(phenylmethoxy)phenyl]-1H-pyrazol-3-yl]-1'-oxo-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L4 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:152682 CAPLUS

DOCUMENT NUMBER: 134:207809

TITLE: Preparation of spiroisindolinepiperidines, spiroisoquinolinepiperidines, spiroisobenzofuranpiperidines, and related compounds as neuropeptide Y antagonists.

INVENTOR(S): Fukami, Takehiro; Kanatani, Akio; Ishihara, Akane; Ishii, Yasuyuki; Takahashi, Toshiyuki; Haga, Yuji; Sakamoto, Toshihiro; Itoh, Takahiro

PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 164 pp.

10/092,549

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

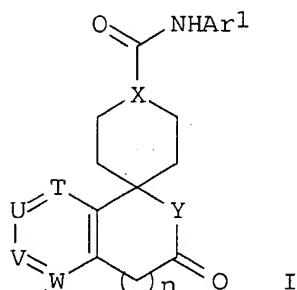
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014376	A1	20010301	WO 2000-JP5427	20000811
W: AE, AG, AL, AM, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000013423	A	20020507	BR 2000-13423	20000811
EP 1204663	A1	20020515	EP 2000-951971	20000811
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
EE 200200082	A	20030616	EE 2002-82	20000811
NZ 517057	A	20030829	NZ 2000-517057	20000811
JP 2002030086	A2	20020129	JP 2000-247145	20000817
JP 3411262	B2	20030526		
JP 2003104884	A2	20030409	JP 2002-271261	20000817
BG 106390	A	20021229	BG 2002-106390	20020206
NO 2002000814	A	20020415	NO 2002-814	20020219
US 2003055251	A1	20030320	US 2002-226225	20020823
PRIORITY APPLN. INFO.:			JP 1999-233573	A 19990820
			JP 2000-137692	A 20000510
			WO 2000-JP5427	W 20000811
			JP 2000-247145	A3 20000817
			US 2000-640784	A3 20000818
			US 2001-983598	A3 20011025
			US 2002-101221	A3 20020320

OTHER SOURCE(S):  
GI

MARPAT 134:207809



AB Title compds. [I; Ar1 = (substituted) aryl, heteroaryl, QAr2; Ar2 = (substituted) aryl, heteroaryl; Q = bond, CO; T, U, V, W = N, (substituted) CH; X = N, CH; Y = (substituted) imino], were prepd. Thus, N-tert-butoxycarbonyl-4-piperidone was refluxed 3 h with PhCH2NH2 in PhMe to give a residue which was stirred with o-iodobenzoyl chloride and Et3N in PhMe at 80.degree. for 2 h to give N-benzyl-N-(1-tert-butoxycarbonyl-1,2,3,6-tetrahydropyridin-4-yl)-2-iodobenzamide. The latter was heated with Pd(OAc)2, Ph3P, K2CO3, and Et4NCl in MeCN at 80.degree. for 6 h to give 2-benzyl-1'-tert-butoxycarbonyl-1',6'-dihydrospiro[1H-isoindole-



10/092,549

1,4'-(5'H)-pyridine]-3(2H)-one. This was converted to N-(4-benzoylphenyl)-3-oxospiro[isindoline-1,4'-piperidine]-1'-carboxamide, (II), which inhibited [125I]peptide YY binding to NPY Y5 receptors with IC50 = 1.2 nM. II drug formulations are given.

IT 328232-41-3P 328232-42-4P 328232-43-5P  
328232-44-6P 328232-45-7P 328232-46-8P  
328232-47-9P 328232-48-0P 328232-49-1P  
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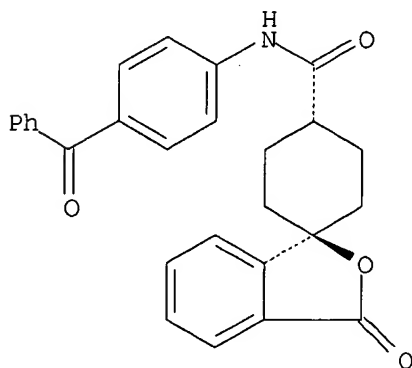
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of spiroisindolinepiperidines, spiroisoquinolinepiperidines, spiroisobenzofuranpiperidines, and related compds. as neuropeptide Y antagonists)

RN 328232-41-3 CAPLUS

CN Spiro[cyclohexane-1,1'-(3'H)-isobenzofuran]-4-carboxamide,  
N-(4-benzoylphenyl)-3'-oxo-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 328232-42-4 CAPLUS

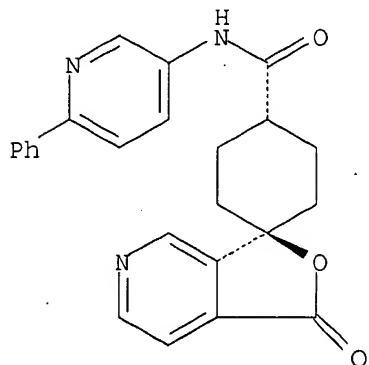
CN Spiro[cyclohexane-1,1'-(3'H)-isobenzofuran]-4-carboxamide,  
3'-oxo-N-(5-phenylpyrazinyl)-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

10/092,549

1'-oxo-N-(6-phenyl-3-pyridinyl)-, trans- (9CI) (CA INDEX NAME)

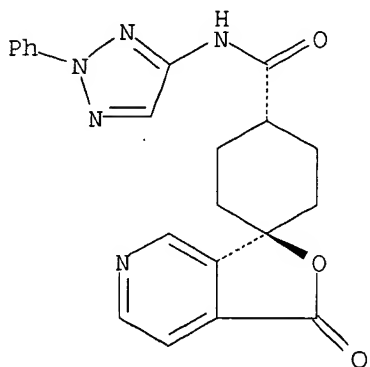
Relative stereochemistry.



RN 328232-99-1 CAPLUS

CN Spiro[cyclohexane-1,3'-(1'H)-furo[3,4-c]pyridine]-4-carboxamide,  
1'-oxo-N-(2-phenyl-2H-1,2,3-triazol-4-yl)-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 328233-32-5P 328233-33-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)

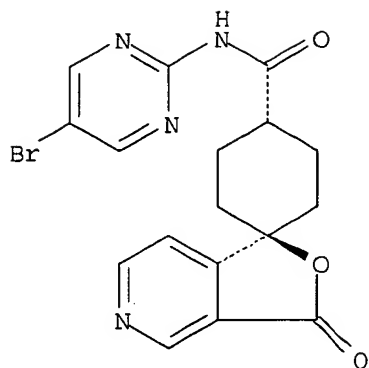
(prepn. of spiroisoindolinepiperidines, spiroisoquinolinepiperidines,  
spiroisobenzofuranpiperidines, and related compds. as neuro peptide Y  
antagonists)

RN 328233-32-5 CAPLUS

CN Spiro[cyclohexane-1,1'-(3'H)-furo[3,4-c]pyridine]-4-carboxamide,  
N-(5-bromo-2-pyrimidinyl)-3'-oxo-, trans- (9CI) (CA INDEX NAME)

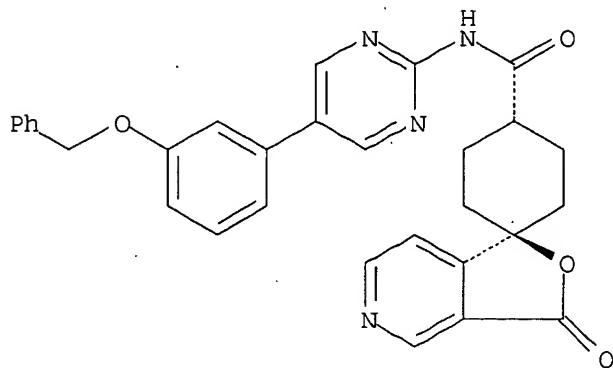
Relative stereochemistry.

10/092,549



RN 328233-33-6 CAPLUS  
CN Spiro[cyclohexane-1,1' (3'H) -furo[3,4-c]pyridine]-4-carboxamide,  
3'-oxo-N-[5-[3-(phenylmethoxy)phenyl]-2-pyrimidinyl]-, trans- (9CI) (CA  
INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 14:35:33 ON 11 OCT 2003)

FILE 'REGISTRY' ENTERED AT 14:35:44 ON 11 OCT 2003

L1 STRUCTURE UPLOADED

L2 1 S L1

L3 207 S L1 FULL

FILE 'CAPLUS' ENTERED AT 14:37:05 ON 11 OCT 2003

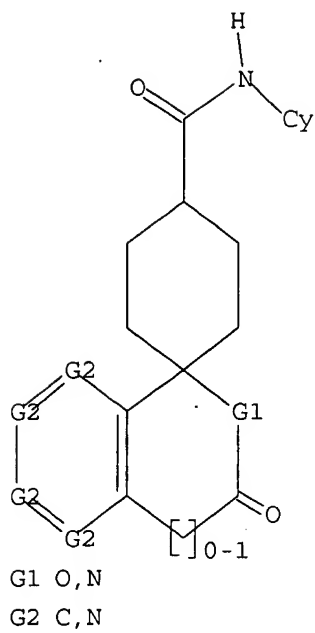
L4 4 S L3

=> d l1

L1 HAS NO ANSWERS

L1 STR

10/092,549



Structure attributes must be viewed using STN Express query preparation.